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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,346	04/29/2005	Terry L. Sheehan	02-40 US	5921
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Varian Inc. Legal Department 3120 Hansen Way D-102 Palo Alto, CA 94304			EXAMINER GAKH, YELENA G	
			ART UNIT 1797	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/533,346	Applicant(s) SHEEHAN, TERRY L.	
	Examiner Yelena G. Gakh, Ph.D.	Art Unit 1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 April 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 14, 15 and 18 is/are allowed.
- 6) ☒ Claim(s) 1-13, 16, 17 and 19-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method comprising the step of incorporating the temperature profile obtained under the conditions recited in claim 2 into LC/MS system, or which comprises the step of performing LC/MS analysis using the temperature profile obtained under the conditions recited in claim 2, does not reasonably provide enablement for the method, which does not comprise one of these steps. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. Obtaining a temperature profile according to a composition gradient profile in LC system is irrelevant to optimizing LC/MS system, unless it is used in LC/MS system either by pre-programming LC/MS system according to the obtained profile, or by performing LC/MS experiment using this temperature profile. Therefore, there is no way to optimize LC/MS system just by measuring a temperature profile according to the gradient profile of the mobile phase, if this profile is not utilized in LC/MS system.

Furthermore, the recitation of claim 2 appears to be the only possible way to obtain the temperature profile that can be used for optimizing LC/MS system according to claim 1, because in order to have a composition gradient profile for the mobile phase, at least two solvents are required to be present in the matrix, and at least two temperature values are required for evaporating the least volatile and the most volatile solvents.

3. Claims 19-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The disclosure specifically directed toward improving API LC/MS, i.e. the system which include optimization parameters for performing LC-mass spectrometry. The specification

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does not disclose any embodiments, which do not comprise MS part of the system. The Applicant is respectfully reminded of the following:

According to MPEP §2163, in particular, "2163.02. Standard for Determining Compliance with Written Description Requirement:

The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)). Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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5. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites in its preamble "a method for optimizing an LC/MS system"; however, in the body the claim recites only obtaining a temperature profile, which varies according to the gradient mobile phase of LC system, which may be totally irrelevant to performing LC/MS, since nothing in the body of the claim is related to performing MS analysis.

Claim 6 recites determining a flow profile without any reference to the temperature profile recited in the parent claim. It is not apparent, as to how the flow profile of claim 6 is related to the temperature profile of the parent claim. The same problem exists for its dependent claims 8-12.

Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: incorporating the temperature profile obtained under the conditions recited in claim 2 into LC/MS system, or performing LC/MS analysis using the temperature profile obtained under the conditions recited in claim 2. These steps are essential for optimizing an LC/MS system.

Claim 19 recites "a heating controlling device for controlling a temperature"; however, it is not quite clear, whether the heating device is an automated device comprising a controlling system for operating according to the pre-programmed temperature profile, or it is any heating device, which can be manually manipulated. In the latter case the apparatus of claim 19 reads on any API LC/MS spectrometer, since any of such spectrometers has a heating device. Since the claim can be read on any API LC/MS spectrometer, comprising a heating controlling device, the examiner interprets the claim in its broadest meaning.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. **Claims 13, 16, 17** are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins et al. (US 2002/0023878 A1) (Collins).

Collins teaches "high-throughput purification process":

"In the present embodiment, the analytical chromatographic parameters comprise a first set of gradient elution parameters associated with gradient elution of the first portion of the chemical mixture through the analytical HPLC column. As one of ordinary skill in the art will understand, **gradient elution separation typically comprises varying a composition of a mobile phase for a gradient time interval and injecting the mobile-phase into a column (e.g., the analytical HPLC column) in accordance with a flow rate. In the present embodiment, a polarity of the mobile phase is decreased in a linear gradient for the gradient time interval.** In the present embodiment, the polarity of the mobile phase is varied by adjusting relative amounts of two or more solvents of different polarity. In particular, the polarity of the mobile phase may be varied by adjusting relative amounts of a more polar solvent A (e.g., water) and a less polar solvent B (e.g., acetonitrile). The mobile phase may also include one or more solvents with amounts that are not varied during the gradient time interval, such as, for example, a relatively small quantity (e.g., 0.05 volume percent) of TFA." (Paragraph [0072]).

The HPLC chromatography is disclosed in the form of LC-MS chromatography (paragraph [0070]). While Collins does not specifically disclose flowing an eluent to API interface, API LC/MS technique is a well known version of LC/MS spectrometry. Therefore, it would have been obvious for a person of ordinary skill in the art to apply Collins' method specifically for API LC/MS spectrometry, as a specific version of LC/MS methods.

9. **Claims 19 is** rejected under 35 U.S.C. 103(a) as being unpatentable over Lubman et al. (US 2002/0039747 A1) (Lubman).

Lubman discloses API LC/MS spectrometer with the heating control device in HPLC (see e.g. paragraph [0113]). While the heating controlling device is not disclosed specifically for

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controlling the gas flow according to the temperature profile, the heating control of the claim is not recited as being pre-programmed for controlling the temperature profile, and therefore Lubman's apparatus is capable of controlling the temperature.

10. **Claim 20** is rejected under 35 U.S.C. 103(a) as being unpatentable over Lubman in view of Collins.

Lubman does not specifically disclose the apparatus which comprises a flow control device. Collins discloses such apparatus for his LC/MS system.

It would have been obvious for a person of ordinary skill in the art to add the flow control device in Lubman's apparatus, because Collins specifically emphasizes importance of a flow control for LC/MS spectrometry.

Allowable Subject Matter

11. **Claims 14, 15 and 18** are allowed. The following is an examiner's statement of reasons for allowance: the prior art does not teach or fairly suggest a method for operating an API LC/MS system according to the steps of claims 14, 15 and 18, specifically by controlling the flow gas according to the temperature profile based on the composition of the eluent flowing o API interface..

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Yelena G. Gakh/
Primary Examiner, Art Unit 1797

11/9/2008